UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,146	02/04/2002	Frederick P. Siegal	10034-004	7266

20583 7590 11/18/2003

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,146	SIEGAL ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with th c rrespondenc address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *020402* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 11-15 are examined in this office action

► *Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm).* The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**

Election/Restrictions

Applicant's election with traverse of Group III in Paper filed on 10/06/03 is acknowledged. The traversal is on the ground(s) that even though group I and III represent distinct and independent inventions, the search and examination of subject matter of both groups would not be a serious burden on the examiner. This is not found persuasive because Group I requires method of treating a disease in a subject by administering to the subject a therapeutically effective amount of interferon producing cells (natural or genetically modified), whereas the method of Group III is a diagnostic method that requires the quantitation of interferon producing cells in a sample obtained from a HIV-infected patient. These inventions have different modes of operations functions and effects (see MPEP 806.04 and 808.01). In instant case the method enumeration of interferon positive cells is performed in-vitro (microscopy, ELISpot or FACS analysis), which have

different modes of operation and protocols as compared to therapeutic method of group I which requires infusion of genetically engineered cells. Thus these inventions are distinct and are of separate uses.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 and 16 -19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10/06/03.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of the invention as claimed encompasses a method of monitoring the progression of any disease or disorder (*pathogenic or non-pathogenic, genetic or environmental*) by measuring number of any interferon producing cells (*any type of cell producing any type of interferons*) obtained from a patient and comparing it to a control sample. At best the specification only discloses evaluation of IFN-α production by total PBMCs or pDC2-depleted, pDC2-enriched mononuclear cells (pages 30-32). The specification further teaches a method of evaluating the number of pCD2-interferon-producing dendritic cells (fig-1 and 2). The specification further disclosed statistical correlation among IFN-a generation, CD4 T-cell counts and viral burden in HIV patients (page 34, sec.8.2; page 40 table-1). However, the specification fails to establish any correlation and/or control sample range for pCD2-interferon-producing dendritic cells, which can be used as a reference range to evaluate the progression of any disease, especially HIV-infection. Similarly the specification fails to establish interferon producing cells reference range (control sample) for any disease, wherein the cell in question has been obtained from any origin (blood, skeletal muscle, cardiac muscle, neuronal skin cells etc).

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to

the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the specification as filed fails to establish the interferon producing cells reference range for any disease (for any type of interferon), wherein the cell in question has been obtained from any origin (blood, skeletal muscle, cardiac muscle, neuronal skin cells etc). It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed invention

since the specification as filed fails to establish a control sample range for all type of interferon producing cells (all type of interferon) to monitor the progression of any disease or disorder (as claimed).

Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of Invention: Invention relates to a method of monitoring the progression of a disease or disorder by measuring the number of interferon-producing cells as compared to a control sample or a previously determined reference range.

Breadth of Claims and Guidance Provided in the Specification:

The scope of the invention as claimed encompasses a method of monitoring the progression of any disease or disorder (*pathogenic or non-pathogenic, genetic or environmental*) by measuring number of any interferon producing cells (*any type of cell producing any type of interferon*) obtained from a patient and comparing it to a control sample. At best the specification only discloses evaluation of IFN-α production by total PBMCs or

pDC2-depleted, pDC2-enriched mononuclear cells (pages 30-32). The specification further teaches a method of evaluating the number of pCD2-interferon-producing dendritic cells by cell sorting techniques (fig-1 and 2). The specification further disclosed statistical correlation among IFN-a generation, CD4 T-cell counts and viral burden in HIV patients (page 34, sec.8.2; page 40 table-1). However, the specification fails to establish any correlation and/or control sample range for pCD2-interferon-producing dendritic cells, which one skill in the art could use as a reference range to evaluate the progression of any disease, especially HIV-infection. Similarly the specification fails to establish interferon producing cells reference range (control sample) for any disease, wherein the cell in question has been obtained from any origin (blood, skeletal muscle, cardiac muscle, neuronal skin cells etc).

State of Art and Predictability: Interferons are the cytokines produced by virus-infected cells that enable neighboring cells to resist virus infection. IFN-α (leukocyte IFN) and IFN-β (fibroblast IFN), the two type 1 antiviral IFNs, are distinct from type 2 IFN-γ produced by effector T cells. Specialized leukocytes, the "natural IFN-producing cells" (NIPCs), were shown to be the chief IFN-α producers in response to enveloped viruses, bacteria, and tumor cells. IPCs express CD4 and major histocompatibility complex (MHC) class II, but lack hematopoietic-lineage markers. Therefore

the nature of IPCs whether they represent dendritic cells or cells of a distinct lineage has been controversial. There is a progressive loss of CD4+ T lymphocytes and functional IPCs during human immunodeficiency virus (HIV) infection. Preservation of IPCs is associated with protection from opportunistic infections, suggesting the importance of IPCs in the host defense (Siegal et al, Science 284:1835-1837, 1999, *ref. of record, see page 1835*). Furthermore, increased frequency and severity of infections in the elderly have been taken as indicative of declining immune function. Dendritic cells (DCs), the most important antigen-presenting cells, play a central role in initiating and modulating immune responses. One type, DC2, arises from precursor plasmacytoid DCs (pDCs), a rare population of circulating blood cells, whose hallmark function is rapid and copious production of interferon-(IFN-a) upon microbial challenge. However there is a significant decrease of the circulating pDCs during ageing in healthy adult humans (Shodell et al Scand J. Imunol 56:518-521, 2002 see page 518). Furthermore the cellular identity of NIPC is the most important issue in the enumeration of NIPC in a particular disease. For example it is important establish whether these cells represent a unique lineage or do they belong to an already defined lineage of cells such as dendritic cells. The developmental pathway of NIPC has not been well characterized. The cellular distribution of NIPC is also not known, since appropriate tissue studies have not been performed to determine

whether the cells are able to move out of periphery and into tissues. Clearly most significant impairment to studies of IFN-a system in human peripheral blood remains the inability to identify the unique NIPC (Fitzgerald-Bocarsly et al Pharmac. Ther. 60:39-62, 1993, *ref. of record see page 56 sec.7*).

In instant case monitoring the progression of any disease or disorder by evaluating the number of IPC in a sample obtained form a subject having any disease or disorder is not routine in the art and without sufficient guidance to a specific disease and its correlation to IPC, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Howell et al (Clinical Immunology and Immunopathology 71(2):223-230, 1994).

The instant claims are drawn to a method of monitoring the progression of a disease or disorder by measuring number of interferon producing cells obtained from a patient and comparing it to a control sample. The claims are further drawn to the method wherein the disease or disorder is the result of HIV infection. In addition the claims are drawn to a method that evaluate the progression of HIV-infection by evaluating the number of interferon producing cells.

Howell teaches a method of monitoring the progression of HIV infection by measuring the number of interferon-producing cells in a sample obtained from HIV patients and comparing the number of interferon-producing cells (NIPC) in the sample with a previously determined reference range (page 225 fig-2). Using ELISpot immuoplaque technique the cited art established that the mean frequency of NIPC among the PBMC for healthy control population was 0.00142 (i.e. 1/703), with a range of 1/200 to 1/3000 (page 228, col.2 para.2). The cited art further teaches that HIV+ patients made significantly less IFN-α in response to UV-HSV as compared to healthy control population. The deficiency was more pronounced in patients with advanced AIDS, and asymptomatic patients had normal levels of IFN-a

production. The ELISpot data indicated that the HIV patients have an average of about fourfold less NIPC among their PBMCs than healthy controls. The cited art further teaches that each NIPC from healthy controls produce on average of 2.0 IU of IFN-a, whereas the cells from HIV+ patients produces on average half this amount (page 228, col.2 para.3). The cited art further teaches that HIV patients with opportunistic infections had significantly fewer NIPC as compared to healthy control population or HIV patients. The cited art further teaches that it is possible that antiviral therapies directed against the opportunistic infections can reverse the IFN-α deficiency in the patients or prevent the patients from progressing to the IFN-α deficient state (page 228 col.2 para. 4). Thus the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be

reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
Patent examiner

JEFFREY FREDMAN
PRIMARY EXAMINER